DOCUMENT RESUME

ED 062 151 SE 013 597

TITLE	Recommendations for the Undergraduate Mathematics Program for Students in the Life Sciences. An Interim Report.
INSTITUTION	Committee on the Undergraduate Program in Mathematics, Berkeley, Calif.
SPONS AGENCY	National Science Foundation, Washington, D.C.
PUB DATE	Sep 70
NOTE	34p.
AVAILABLE FROM	CUPM, P. O. Box 1024, Berkeley, California 94701 (Free)
EDRS PRICE	MF-$0.65 HC-$3.29
DESCRIPTORS	Agricultural Education; Biology; Calculus; *College Mathematics; *Curriculum; *Mathematical Applications; Mathematics Education; Medical Education; Undergraduate Study
IDENTIFIERS	CUPM

ABSTRACT

This report considers the mathematics required by life science students (those with majors in agriculture and renewable resources, all branches of biology, and medicine) who have successfully completed the usual pre-calculus courses. A core is proposed, to include one year of calculus, some linear algebra, and some probability and statistics. Experience in using computers is also recommended. Extensions, including preparation for biomathematics and the use of mathematical models in the life sciences, are also discussed. (MM)

ED 062151

SE 013 597

COMMITTEE ON THE UNDERGRADUATE PROGRAM IN MATHEMATICS

MATHEMATICAL ASSOCIATION OF AMERICA

RECOMMENDATIONS FOR THE UNDERGRADUATE MATHEMATICS PROGRAM FOR STUDENTS IN THE LIFE SCIENCES

AN INTERIM REPORT

SEPTEMBER 1970

RECOMMENDATIONS FOR THE UNDERGRADUATE MATHEMATICS PROGRAM

FOR STUDENTS IN THE LIFE SCIENCES

An Interim Report of the

Panel on Mathematics for the Life Sciences

COMMITTEE ON THE UNDERGRADUATE PROGRAM

IN MATHEMATICS

September, 1970

The Committee on the Undergraduate Program in Mathematics is a committee of the Mathematical Association of America charged with making recommendations for the improvement of college and university mathematics curricula at all levels and in all educational areas. Financial support for CUPM has been provided by the National Science Foundation.

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In its deliberations on this report, the Panel on Mathematics for the Life Sciences has had the benefit of consultation with many life scientists, particularly from the Commission on Undergraduate Education in the Biological Sciences. It is especially grateful for the active assistance of Dr. David Cardus of Baylor College of Medicine, Dr. Fred M. Snell of the State University of New York at Buffalo, and Dr. Otto Schmitt of the University of Minnesota.

George Pedrick, California State College at Hayward, was Executive Director of CUPM, and Gerald Leibowitz, The University of Connecticut, was Associate Director of CUPM during the major part of the study which led to this report.

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1. Introduction

The Committee on the Undergraduate Program in Mathematics (CUPM) has long concerned itself with the problem of recommending suitable mathematics curricula for undergraduate students with a large variety of career goals. In addition to issuing recommendations for the pregraduate training of research mathematicians, students of physics and engineering, and teachers of mathematics at several levels, CUPM has published reports concerning the general curriculum in a small college, programs in applied mathematics, and mathematics for life and social scientists. These reports are entitled, respectively, A General Curriculum in Mathematics for Colleges (GCMC, 1965),* A Curriculum in Applied Mathematics (AM,1966), and Tentative Recommendations for the Undergraduate Mathematics Program of Students in the Biological, Management and Social Sciences (BMSS, 1964).

We shall refer to these three reports frequently in the sequel, using the abbreviations GCMC, AM, and BMSS.

The Panel on Mathematics for the Biological, Management, and Social Sciences was primarily concerned with the mathematics curriculum for prospective graduate students in those fields. Their recommendations were meant to serve as a basis for discussion and experimentation. From these discussions, it became apparent that (1) some of the recommendations would be very difficult for mathematics departments to implement, (2) a different program was needed for the terminal bachelor's degree, (3) the single program presented would not seem to be ideally suited to the diverse fields included in the BMSS disciplines, especially at the advanced level. In response to these findings, CUPM decided to concentrate on individual disciplines and as a first step appointed the present Panel on Mathematics for the Life Sciences (MLS), charged with making recommendations for the mathematical training of the undergraduate life science student, whether or not he goes on to graduate school. (Here, life sciences are taken to mean agriculture and renewable resources, all branches of biology, and medicine.)

The MLS Panel has undertaken, through conferences and extensive consultation with leaders in the biological field, to learn from them what mathematics they consider to be necessary for their students. In particular, the MLS Panel held several meetings with representatives of the Commission on Undergraduate Education in the Biological Sciences (CUEBS). After the biologists had specified the mathematics needed by students of biology, the MLS Panel proceeded to describe mathematics courses that contain this mathematics. This report is the outcome of these consultations and studies. Finally, the MLS Panel held a special conference in which a preliminary draft of this report was submitted to a group of biologists for comment and criticism. The discussions and conferences with the bio-

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*We recommend that the reader of this report have the GCMC report in hand. Copies of this and other CUPM reports can be obtained free of charge by request to CUPM, P.O. Box 1024, Berkeley, California 94701.

logists have emphasized a serious fourth problem: (4) heavy requirements in chemistry, physics, and biology make it difficult for a major in the life sciences to add mathematics courses to his program.

In preparing this report, the MLS Panel considered all four of the problems mentioned above, and it presents herewith its recommendations for a basic mathematics core for life science undergraduate majors (see Part I) and for certain more specialized studies (see Part II).

Part I describes a basic core of mathematics for all undergraduate majors in the life sciences. In Section 2, we describe the level of mathematical preparation on which this core is based. In Section 3, the recommendations for the mathematical core are stated and justified, and in Section 4 we treat some of the principlea and details of implementation of this core.

The MLS Panel feels strongly that every life science major should gain substantial experience with computers (digital, analogue, and hybrid). Although the GCMC report mentions computer experience, we feel that the time is ripe now for a more detailed treatment of the role of the computer in the undergraduate program, especially as it relates to the life science student. This accounts for the greater detail found in Section 5.

Part II outlines certain more specialized studies which this MLS Panel believes will be important for some students in mathematics as well as for some students in the life sciences. Section 6 describes a program for undergraduate preparation for the study of biomathematics at the graduate level. A description of an upper division course focusing on the building of mathematical models in the life sciences and some suggestions for its implementation appear in Section 7.

Since certain of the GCMC courses are cited frequently, we have included their description in Section 8 as an appendix. The entire GCMC report is currently being reviewed, and revised course outlines will be published in due course. It is anticipated that this MLS report will then be reissued in final form.

PART I MATHEMATICS FOR UNDERGRADUATE BIOLOGY MAJORS

2. Background of the Students

In recent years, much effort has been expended to improve mathematics education in the elementary and secondary schools. Several programs of improvement in secondary schools have already had considerable effect and we hope that they will have a great deal more. In particular, we hope that mathematics courses in the secondary school will contain a judicious mixture of motivation, theory, and applications. For the purposes of our discussion, it is assumed that the student is acquainted with both the algebraic and the geometric aspects of elementary functions (see the description of Mathematics 0 in the Appendix); moreover, we assume that the student has been exposed to the idea of a set, mathematical induction, binomial coefficients, and the summation notation. Thus, our discussion applies to students in the life sciences who are prepared to begin their collegiate mathematics with a calculus course, although departments of mathematics may have to offer precalculus courses in order to prepare some students adequately for this program.

Historically, mathematics has been closely allied to the physical sciences, especially to physics. In secondary schools and in elementary undergraduate courses, applications of mathematics have traditionally been limited to the physical sciences. Therefore, it is not uncommon for students whose interests lie in other fields to enroll in a bare minimum of mathematics courses. If students are to possess the prerequisites stated above, proper counseling both in high school and in college is imperative. Students must be made aware of the doors that are closed to them in fields of the life sciences, as well as in the physical sciences and engineering, when they terminate their study of mathematics prematurely. We hope that this message will be transmitted to guidance and counseling personnel, and we urge all concerned to give attention to ways by which counseling of potential life science students can be improved in their locality.

3. The Basic Core: Recommendation and Justification

The Panel on Mathematics for the Life Sciences has considered the problem of recommending a basic core of mathematics courses for students in the life sciences. The prospective life science major, whatever his specialty or career goal, now needs more mathematics than was recognized to be the case a few years ago. As a result of its study, the MLS Panel concludes that the mathematical core for the undergraduate life science major should include one year of calculus, some linear algebra, and some probability and statistics.

More specifically, the MLS Panel believes that this core can be provided by the following courses of the GCMC report: Mathematics 1 (Introductory Calculus, second version), Mathematics 2 (Calculus, multivariable version), Mathematics 3 (Linear Algebra), and Mathematics 2P (Probability and Statistics). In addition, we recommend that each student gain some experience in the use of an automatic computer in the first two years of

study. This might come in the form of a sequence of laboratory exercises (see Section 5) in which algebraic language problems are developed and run. Institutions which do not have computation centers may be able to provide service via remote terminals or through the courtesy of nearby organizations. This permits the use of computing algorithms, lecture demonstrations, or problem assignments in biology and mathematics courses at appropriate times.

The recommendations are consistent with the findings of the two life science commissions sponsored by the National Science Foundation. In Publication No. 18 of the Commission on Undergraduate Education in the Biological Sciences (CUEBS, 3900 Wisconsin Avenue, N.W., Washington, D.C. 20016), "Content of Core Curricula in Biology" (June, 1967), pp. 30-31, we find: "Fourth, we recommend that careful attention be given to relating biology courses to the background of the student in mathematics, physics, and chemistry...in mathematics, at least through the level now generally taught as calculus,...some background in physical and organic chemistry." This recommendation clearly indicates that a full-year sequence of calculus (including multivariable calculus) should be taken by a biology major. In this same publication, the curricula for biology majors at Purdue University, Stanford University, North Carolina State University and Dartmouth College are presented. At three of these institutions, one year of calculus is required in addition to some probability and linear algebra. In the remaining institution, additional calculus is required instead of "finite mathematics" (here taken to mean basic linear algebra with applications--such as Markov chains--and combinatorial probability).

In 1967, the Commission on Education in Agriculture and Natural Resources (CEANAR) charged a committee "to recommend mathematics requirements to be met ten to fifteen years hence in undergraduate curricula for Agriculture and Natural Resources." In its report* this committee chose to state its recommended requirements almost entirely in terms of courses described in the GCMC report. Mathematics 1, 2P and some computer instruction are recommended for majors in all areas covered by CEANAR. Moreover, for students majoring in technology programs, Mathematics 2 and Mathematics 7 (Probability and Statistics) are recommended; to this, students majoring in science programs should add Mathematics 3 and Mathematics 4 (a third course in calculus).

There are other good reasons for recommending this core of four mathematics courses: 1, 2, 3 and 2P. First of all, these are standard mathematics courses, whose broad availability should facilitate implementation. Secondly, this curriculum is flexible enough to accommodate a student who may decide to change his major. For example, if in the first year or two he enters a discipline that involves more mathematics, he will not have lost any time. Thirdly, compressing this material into a shorter three course sequence is unwise from a pedagogical point of view. Very few students are capable of gaining even a minimal mastery of calculus in a one semester course, and at least one semester is needed to cover a significant amount of linear algebra or of probability. Moreover, if a student eventually decides to take more advanced mathematics and still con-

*See "Undergraduate Education in the Physical Sciences and Mathematics for Students in Agriculture and Natural Sciences," pp. 32-35. This report is available from the Division of Biology and Agriculture, the Natural Research Council, 2101 Constitution Avenue, Washington, D.C. 20418.

tinue in the branch of life sciences he originally chose, he will have the appropriate prerequisites. In this connection, we discuss in Section 7 the role of a course in the applications of mathematics to the life sciences for the research-bound student. Since such a course involves relatively advanced mathematics, it will carry certain further mathematical prerequisites beyond the core itself.

Preparation for research in certain areas of biology will demand competence in mathematics equivalent to the Master's degree level. Some biologists have even asserted that a student who has a Bachelor's degree with a major in mathematics and appropriate courses in chemistry and physics would be welcomed as a graduate student in biology, even though he had had no courses in biology. Further development of this line of thought is found below in Section 6 on biomathematics.

Although the MLS Panel feels that an offering to life science students of less than four semesters of mathematics course work will not meet the objectives laid out by the life scientists whom we have consulted, we must recognize that this amount of mathematics is more than will be accepted by some of them as a requirement for all undergraduate life science majors. We have been urged to consider what can be done with three courses. Any three course program will lose some of the desirable features described in the last paragraphs. We present several options of three courses and point out some of the advantages and shortcomings of each:

(1) Mathematics 1, 2, 3;
(2) Mathematics 1, 3, and 2P;
(3) Mathematics 1, some appropriate interweaving of 2 and 3, and 2P;
(4) Mathematics 1, 2 and one semester of finite mathematics;
(5) An integrated three-semester sequence, specifically designed for life science students, and built around finite mathematics, calculus through multivariable calculus, probability and statistical inference.

It may be well to observe that each of the above options could lead to completion of the core in graduate school, if this were desired. This could be done with standard courses in the case of options 1 or 2 or with one or more special courses in the case of other options.

Some features of the options are highlighted in the following table:

	Number of special mathematics courses required	Number of core subjects omitted entirely	Full year of calculus included
Core	0	0	Yes
Option 1	0	1	Yes
Option 2	0	1	No
Option 3	1	0	No
Option 4	1	0	Yes
Option 5	3	0	No

The first column measures to some extent the extra load placed on the mathematics department by each option. The offering of each special course involves planning and coordination activities and in a small institution may have a high cost per student because of limited enrollment.

Any option involving special courses inevitably raises the possibility of additional course work (or equivalent thereof) being required to provide the proper prerequisites for further study in mathematics. The severity of this effect can be assessed only in the context of a given institution, a given spectrum of courses, and some designated group of students at a given skill level.

Column 3 relates to the remark that offering less than a full year of experience in calculus seems to be insufficient.

The MLS Panel feels that option 1 is the least undesirable, since 1) probability can be added by many students as an elective, 2) this sequence is easier for most mathematics departments to staff than one involving probability, and 3) many schools now offer linear algebra as an integral part of the calculus sequence. Option 2 is considerably less desirable than option 1, since it omits multivariable calculus, a topic that the Panel feels is vital to modern biology (cf. the previous reference to CUEBS Publication No. 18).

Options 3, 4 and 5 share the disadvantage of having no efficient continuing mathematics course which can be used to complete the core material.

Options 3 and 4 may be suitable for larger institutions in which the mathematics and biology departments can work out arrangements for an additional elective special course which would complete the core. If many departments were to adopt one of these options, graduate departments might choose to <u>require</u> that the core be completed in graduate school. Care must be exercised in implementing option 3 to include topics in calculus that are needed in physics and chemistry prerequisites to biology courses.

The essential feature of option 5 is to construct a three-semester sequence, illustrated by life science examples and containing essential material from the calculus, while interweaving some probability, statistics, and linear algebra in an integrated format. This option is perhaps the least desirable for undergraduates. However, in situations where there are substantial numbers of students who have not had appropriate mathematics courses by the time they begin graduate work in biology, the departments of biology and mathematics may wish to collaborate in designing special programs. It is more important for a graduate biology student to understand the basic concepts of the mathematics he uses than to develop the computational skills needed by a physical scientist or engineer. By taking advantage of the maturity, strong motivation, and established field of interest of these students, satisfactory programs (such as option 5 above), stressing the understanding of these mathematical concepts, could be designed in such a way as to require less time than the standard undergraduate courses.

Such cooperation involving another department with the mathematics department has proved successful in the past. This was particularly true in some areas of the social sciences, where the demand for such programs eventually diminished when the great majority of entering graduate students came with a sufficient mathematical background. The research needs of some biology departments have motivated them to hire biomathematicians, who could participate in teaching the graduate programs envisioned here.

4. The Basic Core: Implementation

The MLS Panel recommends that all life science majors be required to complete two semesters of calculus and one semester each of linear algebra and probability (including some statistics). These courses, Mathematics 1 and 2, Mathematics 3 and Mathematics 2P, are discussed in detail in the GCMC report. In many undergraduate curricula, these courses must serve many needs: prospective biology majors find themselves in the same classes with students from a wide variety of disciplines (such as engineering, economics, business administration, one of the physical sciences, or even mathematics). When this is the case, it is unlikely that special emphasis on biological applications will be featured in any part of this four course program. A few institutions, however, can afford to present all, or some part of, this core program exclusively for students whose main interests lie in the life sciences. We do not address ourselves to the task of making detailed recommendations to this group since we feel that an institution offering a special mathematics core for life scientists will wish to take advantage of local features and design a hand-tailored program. Between these extremes, we find institutions able to give varying amounts of special attention to life science orientation in the mathematics core. Our suggestions below are directed primarily to this group. We expect that there will be considerable latitude in the extent and manner that these recommendations are utilized.

The life science major should be given more consideration than has been the custom in the past, even by the first group of institutions that cannot afford to provide special courses or sections of courses. Traditionally, the applications given in calculus, for example, are almost exclusively chosen from the physical sciences. With the rapid growth of the life sciences, it is only reasonable that increased emphasis be given to illustrative examples from this field, even in a calculus course in which the interests of most of the students lie elsewhere.

We now proceed to our comments on the modifications necessary to make the core courses more suitable to the needs of the life science students.

MATHEMATICS 1 - INTRODUCTORY CALCULUS

The GCMC report contains two outlines of this course, differing primarily in whether the definite integral is introduced at the beginning or in the middle of the course. We prefer the second outline, which is included in the Appendix to this report.

MATHEMATICS 2 - MATHEMATICAL ANALYSIS

Again, the GCMC report contains two outlines for this course. The first version completes single variable calculus in Mathematics 2 and multivariable calculus is studied in the corresponding version of Mathematics 4, whereas the second version introduces geometric vectors and multivariable calculus in Mathematics 2. We recommend that the multivariable version of Mathematics 2 be used because of its obvious relevance to the life sciences. (See the CUEBS recommendations for work in physical chemistry; this clearly uses partial derivatives, differentials, and other concepts from multivariable calculus.) In addition, the multivariable version, if taught suitably, will help to develop and reinforce the student's geometric intuition. We hope that suitable textbooks for this course will be available.

MATHEMATICS 2P - ELEMENTARY PROBABILITY

We recommend that Mathematics 2P be given as stated in the GCMC report, with the following comments:

(1) With respect to (a) of the GCMC description, the introduction of the probability axioms should be properly motivated by the frequency interpretation (see Hodges and Lehmann, Basic Concepts of Probability and Statistics) in order to connect these concepts with the empirical traditions of the life sciences.

(2) With respect to sections (b) and (c), some time could be saved by merging the sections so that the Poisson and normal distributions would be introduced as limits of the binomial distribution. For the normal approximation, we feel that the most efficient presentation--both in consideration of time spent and student understanding--would be to discover numerically that a sequence of binomial cumulative distribution functions, after the usual normalization, tends to the normal distribution (see Mosteller, F., Rourke, R.E.K. and Thomas, G.B., Jr., Probability with Statistical Applications).

(3) As a generalization of sequences of Bernoulli trials, we feel that two-state Markov chains should be included in the course. The presentation of these could begin in the discussion of conditional probability in section (a). A solution for the limiting distribution of the process and a numerical demonstration of convergence to this limit should then follow the other limit theorem discussions, taking up one or two lessons.

(4) If Mathematics 3 is included as a prerequisite for Mathematics 2P, topics such as the Markov process in (3) can be presented more efficiently and in greater depth in matrix form.

A modified course description of 2P appropriate for students in the life sciences can then be given as follows:

(a) Probability as a mathematical system (11 lessons) Variability of experimental results, sample spaces, events as subsets, probability axioms and immediate consequences, finite sample spaces and equiprobable measure as a special case, random variables (discrete and continuous), conditional probability and stochastic independence, Bayes' formula. Sequences of independent Bernoulli trials, two-state Markov chains.

(b) Probability distributions (15 lessons) Characterization of probability distributions by density and distribution functions, illustrated by the binomial and uniform distributions. Expected values, mean and variance, Chebychev inequality, Poisson distribution introduced as approximation to the binomial, normal approximation to the binomial approximation to the binomial, normal approximation to the binomial and Central Limit Theorem, stationary distribution of a simple Markov chain, law of large numbers, discussion of special distributions motivated by relevant problems in the life sciences.

(c) Statistical inference (13 lessons) Concept of random sample, point and interval estimates, hypothesis-testing, power of a test, regression, examples of nonparametric methods, illustrations of correct and of incorrect statistical inference.

MATHEMATICS 3 - LINEAR ALGEBRA

Linear algebra provides another opportunity for the instructor to use and further develop the student's geometric intuition and visualization. Whenever possible, the material in this and the other courses should be related to the student's experience and intuition. Of the two versions given in the GCMC report, we recommend the first, which is reproduced in the Appendix to this report, with the following modifications and comments.*

(1) To allow time for more complete treatment, including flow charts for Gaussian elimination and computer solution using programs already in the library of the computation center, expand topic (a) from 5 to 9 lessons. Add the topics of addition and multiplication by scalars for matrices and vectors (regarded as column matrices).

(2) Reduce topic (c) to 8 lessons and topic (e) to 12 lessons to compensate for the increase for topic (a).

(3) In topic (d) it does not seem desirable to attempt a development of determinants complete with all proofs. What seems reasonable is a statement of the main theorems and enough practice with evaluation

*A linear algebra course that incorporates many such modifications is described as Mathematics L in the CUPM report, A Transfer Curriculum in Mathematics for Two Year Colleges.

of determinants to enable the student to handle similarity theory for low dimensions.

(4) It is doubtful that all of the topics in (e) can be covered in a three-hour course. Except for classes with highly selected students it seems likely that either some topics will have to be omitted altogether or that certain topics will have to be presented without proofs of all theorems.

(5) For a four-hour version of Mathematics 3, we suggest that the list of optional topics also include:

<u>Further geometric applications</u>. Projections and components. Length of a vector, angle between vectors. Vectors in mechanics.

<u>Linear inequalities</u>. Convex sets. Optimization of linear functions over convex polyhedra. Examples of linear programming problems. Matrix representation of linear programming problems and the simplex algorithm.

However, "small vibrations of mechanical systems" might be omitted from the list of optional topics suggested in GCMC, since it has only limited relevance for biologists.

5. Recommendations for Computing

Automatic Computing

We recommend that every undergraduate in the life sciences have some contact with an automatic digital computer, and that this contact begin as early as possible in his program of study. Among the many bases for this recommendation are: that many mathematical models in the life sciences, as witnessed by the current technical literature, are procedural in nature and are best studied with the computer; that many analytic techniques of experimental biology are of practical value only when applied with an automatic computer; and that the automatic computer could play an important role in undergraduate biology lectures and laboratory if the students were prepared to make use of it.

This recommendation is stated separately from our recommendation of a CORE mathematics program for the life sciences student because we feel that experience in automatic computing will become part of a general liberal arts requirement rather than part of a major in either biology or mathematics. In many colleges a first course in computing is not the responsibility of the mathematics department but of a computer science department or a department in which computer applications are already numerous. As applications in subject-area courses increase, the need for an introduction to computing separate from the courses in biology, chemistry, mathematics, and physics may disappear.

CUPM has established a panel to consider instruction in computer science and the use of computers for instruction in mathematics. Our re-

commendations may be used to select options from their recommendations when they become available and to set an amount of experience appropriate for the biology major.

It should be noted that our basic recommendation in automatic computing is minimal. For example, the recommended experience does not include the introduction to analog or to hybrid analog-digital computing, and it includes only the briefest view of the complex problems of numerical analysis. We hope that some analog experience could be gained in advanced biology laboratory work. We also urge that the student be cautioned against the misuse of computing techniques, to avoid any tendency toward confusing the mastery of a programming language with an adequate knowledge of mathematics.

We suggest two alternatives for a one semester course by which this computing experience can be gained. These are described in detail in Section 9. The first alternative is an informal program of weekly lectures and discussions of one hour extending through the freshman year, supplemented by a large number of assigned programming exercises to be developed and run at the student's convenience. It would amount to about one half a semester course for which credit might or might not be given. The second is a formal three semester hour course with five or six assigned programming exercises, to be taken normally in the sophomore year. These suggestions will be stated more completely, but first it seems proper to point out the advantages and problems of the two approaches.

Basic computer programming skills have commonly been acquired through programs of self-instruction. Many computer scientists feel that it is best to provide the student with a computing facility, some reference manuals as to its use, an introductory lesson or two, and then to stay out of his way as he practices by developing programs which are of particular interest to him or are relevant to his other studies. They would not give formal academic credit for this work. We would temper this plan by continuing the lessons or discussion periods beyond the most basic introduction and assigning some specific programs to ensure that the student is exposed to various classical and valuable computing techniques. Even with this modification, the plan has the obvious advantage of not making significant demands on either faculty or student time, an important factor considering the already heavy required curriculum in the life sciences. It reasonably could, in fact, be carried out without academic credit. Unfortunately, the student freedom which permits this implies a lack of control over facility usage, so this alternative can prove expensive in machine charges.

The second alternative, a formal semester course introducing the student to computing, has the disadvantage of adding to an already exacting schedule. A most troublesome additional problem is that we do not feel that the introductory course in many computer science programs is appropriate to students in the life sciences. In that they are planned to set the foundation for further work in mathematics or computer science, they often do not cover computing applications adequately. The course we propose may, therefore, add an additional load on the mathematics faculty, particularly distasteful because of its partial redundancy. A formal

course has two powerful advantages, however. The students will be brought to a higher level of competency and the machine charges per student can be kept relatively low. This applied computing course could be relevant to fields beyond the life sciences, of course, and could be planned to serve all undergraduates not intending to specialize in computer science.

Continuing the Computing Experience

Given the contact with computers which we recommend, the student will be able to use the computer to extend his studies both in mathematics and in the life sciences. Experience has shown that he will, in fact, do so. It is important, therefore, that facilities be available to support this use. While accurate estimates of potential use are impossible, many students will continue computing at about the rate begun in the introductory course if given a chance.

Of importance in taking proper advantage of the student's computing experience is the use of computing exercises and demonstrations whenever relevant in the regular biology curriculum. We point out that the relevance is striking in many areas. For example, a course in population genetics could use a computing facility as a regular laboratory instrument, and some topics such as genetic drift are difficult to present without the computer. Too often, the student will recognize this value before the instructor. It is essential that every effort be made to introduce the potential of applied computing, as well as all other mathematical techniques, to the life science faculty. Among the possible means for this faculty education are: the involvement of the life science faculty in the program of computer instruction, the preparation and distribution of materials and understandable manuals on local computing facilities, the preparation and distribution of computer demonstration and laboratory materials for specific courses, and most important, a demonstration of interest by the mathematics or computing faculty in biological research along with patient collaborative effort with life scientists.

PART II SPECIALIZED STUDIES

6. Undergraduate Preparation for Biomathematics

The present state of biomathematics is such that one cannot expect to study this subject as an undergraduate. The best that can be expected of an undergraduate curriculum is to provide the student with a strong background in mathematics, physics, chemistry, and biology as preparation for graduate study. Indeed, because of its dependence upon the other sciences, biology may be emphasized the least in the undergraduate program and then, presumably, the most in the graduate program. In most colleges, the undergraduate who is enrolled in such a program will be regarded as a major in mathematics.

Before going into details concerning the mathematics component, we consider some general principles on which a biomathematics program should be based.

(1) About one-third of the student's undergraduate curriculum will be devoted to the mathematical sciences, including statistics and computing. A second third will be devoted to physics, chemistry, and biology, and the remainder to the humanities and social sciences to fulfill degree requirements.

Since the student will normally be a major in mathematics, it is important that departments of mathematics allow their majors to choose electives freely in the biological sciences.

(2) Many institutions give several different versions of basic courses in the sciences. The crucial difference is usually the extent to which mathematics is used. It is vital, therefore, that the student plan his program so as to take the most sophisticated version of each course that is available. This injunction applies especially to courses in physics and in physical chemistry.

(3) Very few universities have a department of biomathematics. Most graduate students who study this subject will be enrolled in some life science department. It is essential, therefore, that the undergraduate program of such a student include enough courses in biology for him to gain admission to a graduate program in a life science area. This need not imply that the undergraduate program must contain very many courses in biology. Many leading life science departments will admit a person with as strong a background in mathematics and chemistry as is contemplated here if he has had as few as four semester courses of undergraduate biology and some may even require no undergraduate biology.

(4) It is neither practical nor desirable for a student to make an irrevocable commitment to a particular specialty early in his college career. As was stated in the preceding paragraph, a student who elects the program that is being presented here should be qualified for admission to a graduate life science program. He may then choose to specialize in some area of biology other than biomathematics. On

the other hand, he may decide to do graduate work in mathematics only. By adding a substantial course in abstract algebra to the program described below, he should become eligible for admission to most graduate departments of mathematics.

(5) Of the natural sciences, chemistry will receive the greatest emphasis. Courses in organic chemistry and the strongest possible course in physical chemistry will certainly be included in the program; biochemistry may be also included, although some schools prefer to introduce this topic at the graduate level.

With these considerations in mind, we now turn to the mathematics in this program. The computer experience and the core of four mathematics courses discussed in Sections 4 and 5, as well as in the GCMC report, form the foundation of this preparation. To this we add semester courses in Calculus, Advanced Multivariable Calculus, Statistics and Probability, and a two-semester sequence of Real Variable Theory, as described in Mathematics 4, 5, 7, 11, and 12 in the GCMC report. The GCMC Mathematics 10, preferably in the version described in Section 7 below, and a Numerical Analysis course (see Mathematics 8 in the GCMC report) should be included.

A biomathematician will need to know more mathematics than is presented in this program. For example, he will have only a touch of differential equations in Mathematics 2 and 4, and will ordinarily need considerably more probability and statistics than is covered in Mathematics 2P and 7. Thus, his graduate program will include additional work in mathematics, although it will consist predominantly of biology. A biomathematics student (as well as other biology graduate students) may wish to follow a plan that is currently used in many other graduate fields: electing one mathematics course each term until the Master's degree requirements in mathematics are met. A few biomathematicians may wish to include course preparation for the Ph.D. degree both in mathematics and in the life sciences.

7. A Course in Applications of Mathematics in the Life Sciences

A course in applied mathematics (Mathematics 10) is briefly described in the GCMC report. The essential feature of this course is "model-building and analysis" coupled with appropriate interpretation and theoretical prediction. The philosophy of this approach to applied mathematics is well stated on pages 66 and 67 of the GCMC report, and we recommend the reader's careful attention to that material in order to establish the necessary point of view for consideration of a course entitled Introduction to Applied Mathematics: Life Sciences Option.

Two versions of a model-building course are developed in detail in the AM report. The first is designed for students who have a particular interest in the physical sciences and engineering, while the second is more concerned with those parts of mathematics which are involved in such subjects as linear programming, theory of games, queueing theory, simulation, etc.--in short, with subjects that are classified under the title of

"operations research." It seems appropriate now to consider a third version designed for students with a particular interest in the life sciences.

In much the same way as in the description of the operations research option given in the AM report, applications of mathematics in the life sciences may be classified basically into two broad categories, deterministic and stochastic. Moreover, a third category should also be added, that of mixed models, wherein the particular phenomenon under consideration may be modeled in either deterministic or stochastic fashion.

Specific prerequisites for a life sciences version of Mathematics 10 will vary according to which topics are studied, but in any case they include the basic core, supplemented suitably, -- usually with additional work in calculus and differential equations (Mathematics 4 and 5) and perhaps with additional work in probability and statistics (Mathematics 7).

One feature of life science models is that the mathematics used tends to be either almost trivial or relatively advanced; good "junior level" models seem hard to find. Thus, for the present, successful offering of a life science version of Mathematics 10 would seem to call for an instructor who is well qualified both in mathematics and in the life sciences. Moreoever, this instructor should be broadly interested and knowledgeable in applied mathematics and, in particular, in model-building.

The AM report recommends that, in the absence of such a member of the mathematics faculty, Mathematics 10 should not be offered. It has been found in a number of institutions, however, that a viable alternative may be obtained through a joint effort of an interested member of the mathematics faculty and specialists in various other disciplines. Both mathematics and biology can thus be adequately represented and the essential feature of strong motivation is present. An undergraduate seminar led jointly by such a faculty team, with models being proposed by the members of the class, has been found to work well in practice. A format suitable for this purpose has been described by S. A. Altman ("A Graduate Seminar on Mathematics in Biology." CUEBS News, Vol. V, No. 1, October, 1968, pp. 9-10).

An institution with a strong, modern biological sciences department should be able to offer a course such as that suggested above. This is especially true if the life sciences faculty are interested in bringing in mathematical ideas and there is also present at the institution a mathematics cadre interested in the applied mathematical sciences. Several members of the MLS Panel have had some experience in offering courses based on model-building in both physical and life sciences. Such an approach revolves around an artful use of the case study method, with the class thereafter pursuing the mathematical structure, detective story fashion, wherever it may lead. Usually the mathematical structure itself is developed en route only to the extent that is demanded by the model, although appropriate avenues are of course indicated to the students for following up any particular portions of the mathematics that may especially interest them.

A broadly ranging bibliography of source materials for courses of this kind in the mathematics of the life sciences has been prepared by the MLS Panel and is available free of charge from CUPM upon request. Write to CUPM, P.O. Box 1024, Berkeley, California 94701 asking for the Mathematics 10LS bibliography.

We conclude this section with a few general comments concerning mathematical models in the life sciences.

Model construction consists, for the mathematician at least, of laying down an appropriate axiom system, either as a formal set of axioms or by means of a system of defining equations. Equations of motion in physiology and biophysics, linear algebra formulations of protein sequences or of population state vectors, dynamical systems describing population interactions, combinatorial models of genetic phenomena or of macromolecule configurations are all instances of such axiom systems. Once an appropriate mathematical structure (i.e., a set or sets with operations) has been specified, the further analysis proceeds within the mathematical structure, emerging at certain strategic times with interpretations or theoretical predictions drawn from the mathematical deductions themselves. To the extent that these conclusions are in accord with those aspects of the actual phenomenon that are regarded as significant in that context, so, too, may the original mathematical model be regarded as a good one. One of the virtues of such a procedure, as noted in the GCMC report, is that "the attempt to build a satisfactory mathematical model (often) forces the right question about the original situation to come to the surface." It is clear, therefore, that the modeling process is often one of successive approximations, hopefully convergent to a sound theory at some stage. An essential part of the instructor's responsibility would seem to be conveying to the life sciences student the realization that once an appropriate mathematical structure has been determined via axiomatization, he can work strictly within this mathematical structure, to come back in the end with certain interpretations and theoretical predictions relevant to the particular life science phenomenon under consideration. All too often there seems to be what amounts to almost a mental block in many biologists' thinking that precludes their leaving the realm of empirical laws and statistical description (mathematics as curve-fitting) to work within the mathematical structure itself. The great significance of this latter mode of procedure for the astonishing growth of the physical sciences during the past half century has been well described by Mostow, Sampson, and Meyer (Fundamental Structures of Algebra, McGraw-Hill, 1963, Preface) in the following terms:

> "The great evolution of the physical, engineering and social sciences during the past half century has cast mathematics in a role quite different from its familiar one of a powerful but essentially passive instrument for computing answers. In fact that view of mathematics was never a correct one...Its inadequacy is becoming increasingly apparent with the growing recognition that mathematics is at the very heart of many modern scientific theories--not merely as a calculating device, but much more fundamentally as the sole language in which the

theories can be expressed. Thus mathematics plays an organic and creative part in science, as a limitless source of concepts which provide fruitful new ways of representing natural phenomena."

The objective of the proposed course in applications of mathematics in the life sciences is to develop in students the capability to utilize these powerful mathematical methods in the fashion indicated above.

PART III APPENDICES

8. Course Outlines for GCMC Courses 0, 1, 2, 3, 2P.*

Mathematics 0. Elementary Functions and Coordinate Geometry.

(3 or 4 semester hours)

a. Definition of function and algebra of functions. (5 lessons) Various ways of describing functions; examples from previous mathematics and from outside mathematics; graphs of functions; algebraic operations on functions; composition; inverse functions.

b. Polynomial and rational functions. (10 lessons) Definitions; graphs of quadratic and power functions; zeros of polynomial functions; remainder and factor theorems; complex roots; rational functions and their graphs.

c. Exponential functions. (6 lessons) Review of integral and rational exponents; real exponents; graphs; applications; exponential growth.

d. Logarithmic functions. (4 lessons) Logarithmic function as inverse of exponential; graphs; applications.

e. Trigonometric functions. (10 lessons) Review of numerical trigonometry and trigonometric functions of angles; trigonometric functions defined on the unit circle; trigonometric functions defined on the real line; graphs; periodicity; periodic motion; inverse trigonometric functions; graphs.

f. Functions of two variables. (4 lessons) Three-dimensional rectangular coordinate system; sketching graphs of $z=f(x,y)$ by plane slices.

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*All of the course outlines in this section, taken verbatim from the original GCMC Report of 1965, are currently under review by CUPM.

Mathematics 1. <u>Introductory Calculus</u>. (3 semester hours) (A second version)

<u>Differential Calculus</u>

a. <u>Introduction</u>. (7 lessons) The ideas of the differential calculus are introduced by the intuitive solution of an extreme value problem. The slopes of the graph of x^2 and of a general quadratic function are calculated. Velocity and rate of change. Calculation of derivates of $1/x$, $\sqrt{x}$; derivative at $x=0$ of $f(x)=x \sin (1/x)$ for $x>0$, $f(0)=0$, attempted inconclusively.

Limit and approximation. Limits of sums, products, quotients. Statements of extreme and intermediate value theorems. (Pictorial motivation; no epsilonics.)

b. <u>Technique and applications of differentiation</u>. (14 lessons) Differentiation of linear combinations, products, x^n, polynomials, quotients, rational functions. Concept of inverse function; derivatives of inverses, $\sqrt{x}$, $\sqrt[n]{x}$, rational powers. Vanishing of the derivative at an interior extremum, idea of global and local extrema. Theorem that $f(x)$ has an interior extremum on (a,b) for continuous f such that $f(a)=f(b)$ and theorem that between successive extrema a continuous function is strongly monotone (pictorial demonstrations using extreme and intermediate value theorems). Location of extrema at endpoints of the domain or points where the derivative fails to exist, or at the zeros of the derivative. Solution of extreme value problems. Curve sketching, use of sign of 1st derivative, 2nd derivative. Sign tests for interior extrema. Derivatives of circular functions. Inverse circular functions. Chain rule. Derivatives of implicitly defined functions. Tangent and normal. Law of the mean (pictorial approach), tangent as best linear approximation.

Integral Calculus

c. Area and integral. (8 lessons) Area as limit of Riemann sums, idea of integral, integrable function. Squeeze by upper and lower sums, error estimates for monotone and piecewise monotone functions. Integrals of af, $f+g$. Interpretation of integral as signed area. $\int_a^b + \int_b^c = \int_a^c$. Integral as function of upper endpoint, derivative of "indefinite" integral. Fundamental theorem.

d. Applications. (6 lessons) Volume of solid of revolution; falling body problem. Definition of log x as integral; exponential function. Differential equation for exponential function; growth and decay. Differential equation for sine and cosine; uniqueness of solution to initial value problem; simple periodic phenomena.

e. Techniques of integration and applications. (4 lessons) Simple substitutions. Integration by parts.

Mathematics 2. Multivariable Calculus (3 or 4 semester hours)

a. Vectors in three dimensions. (6 lessons) Scalar and vector products. Equations of lines and planes. Applications to geometry and physics. Vector-valued functions of a real variable, curves, derivative, tangent and velocity, arc length.

b. Real-valued functions of several variables. (12 lessons) Graphical representations, level curves and surfaces. Surfaces of the form $F(x,y,z) = \text{constant}$, quadric surfaces. Limits, continuity, partial derivatives. Differentiable functions, gradient. Differential. Chain rule, tangent plane to a surface, normal. Related rates. Directional derivative, gradient as maximal increase vector of the function and as

normal to level surfaces. Repeated partial derivatives, Taylor's theorem with remainder. Approximations, estimates of the remainder.

c. Integration. (9 lessons) Definition of the integral $\int f(x)dm$, existence, interpretation as area, volume, mass, mean. Numerical evaluation of the integral. Centroids, moments. Evaluation by repeated simple integrals. Applications. Cylindrical and spherical coordinates. Curve integrals. Applications, potential.

d. Differential equations. (12 lessons) Tangent fields given by $y' = f(x,y)$. Meaning of solution curves. Picard's method for establishing existence. Numerical step-by-step solution. Systems $y_i' = f_i(x, y_1, \ldots, y_n)$, numerical solution. Special case $y' = f(x)$. Special numerical methods; trapezoidal rule, Simpson's rule. Equations of the form $Mdx + Ndy = 0$, variables separable, exact differentials, integrating factors. Linear differential equations of first order.

Mathematics 3. Linear Algebra (3 or 4 semester hours)

a. Linear equations and matrices. (5 lessons) Systems of linear equations, equivalence under elementary row operations, Gaussian elimination, matrix of coefficients, row reduced echelon matrix, computations, solutions, matrix multiplication, invertible matrices, calculation of inverse by elementary row operations.

b. Vector spaces. (6 lessons) Vector spaces abstractly defined. Examples. Linear dependence and independence. Linear bases and subspaces, dimension. Inner product, length, angle, direction cosines, applications to line and plane geometry.

c. Linear mappings. (10 lessons) Mappings, linear mappings, kernel and image of a map. Rank of a map. The linear map associated with a matrix. Representation of linear maps by matrices, composition of maps and multiplication of matrices. Algebra of linear mappings and matrices. Change of basis in a linear mapping, similar matrices.

d. Determinants. (4 lessons) Definition of a determinant of a square array, properties of determinants. Cramer's rule. Inverse of a matrix. Determinant of transposed matrix and of the product of two matrices.

e. Quadratic forms. (14 lessons) Symmetric matrices and quadratic forms. Quadric surfaces. Effect of linear transformation. Rational reduction to diagonal. Invariance of index, positive definiteness. Inner product, orthogonal bases, Gram-Schmidt orthogonalization. Orthogonal expansions and Fourier rule. Orthogonal reduction of 2×2 quadratic form, application to plane conics. The general case, orthogonal reduction, characteristic roots and vectors, invariance. Calculation of characteristic roots and vectors. Cayley-Hamilton theorem, trace, discriminant and other scalar invariant functions. Applications to analytic geometry.

This completes 39 lessons for three semester hours. For further applications or in a four semester hour course one may include the following topics.

f. Vector cross product. (4 lessons) Definition and geometric interpretation, algebraic properties. Uses in line and plane geometry.

g. Differential calculus of inner product and cross product. (5 lessons) Differentiation of vector products, applications to curves, arc length, curvature, normal and binormal, torsion. Angular velocity, angular momentum.

h. Groups of symmetries. (6 lessons)

or

Small vibrations of mechanical systems. (6 lessons)

Mathematics 2P. Probability (3 semester hours)

a. Prcbability as a mathematical system. (9 lessons) Sample spaces, events as subsets, probability axioms, simple theorems, finite sample spaces and equiprobable measure as a special case, binomial coefficients and counting techniques applied to probability problems, conditional probability, independent events, Bayes' formula.

b. Random variables and their distributions. (13 lessons) Random variables (discrete and continuous), probability functions, density and distribution functions, special distributions (binomial, hypergeometric, Poisson, uniform, exponential, normal...), mean and variance, Chebychev inequality, independent random variables, functions of random variables and their distributions.

c. Limit theorems. (4 lessons) Poisson and normal approximation to the binomial, Central Limit Theorem, law of large numbers, some statistical applications.

d. Topics in statistical inference. (7-13 lessons) Estimation and sampling, point and interval estimates, hypothesis-testing, power of a test, regression, a few examples of nonparametric methods.

9. Course Outlines for an Introduction to Computing

Following are outlines of programs for the two alternatives suggested in Section 5.

Introduction to Computing: Alternative 1

The course is comprised of weekly or biweekly one hour lecture and discussion meetings and ten or more student programming exercises. It is set primarily for freshmen, although if done with informality, it could involve the entire life science community, including the faculty. The prime goal is the development of basic applied programming skills in an algebraic language. There is little concern for the logical organization of the machine or detailed representation of information in the computer.

Materials

1. An introduction to a common algebraic language, such as FORTRAN, PL/I, ALGOL, or the conversational languages BASIC, CAL, JOSS.
2. A reference for elementary numerical methods.
3. A reference for statistical methods.
4. A reference for simulation and other general problem solving techniques.

Facilities

Computing facilities will be required to handle the submittal of approximately 60 batch process jobs of very short duration per student over the period of the course. If a time-shared computing facility is available, about 20 to 25 console hours will be required equivalently.

The conversational use of a time-shared facility is to be preferred from the point of view of efficient use of student time.

Faculty

In order to assure relevance of the exercises to the life sciences, it would be desirable for an instructor from the life sciences faculty to handle the lectures and discussions for the life science students in this course, initially, with the advice and assistance of a member of the mathematics or computer science faculty. This would also serve as a logical entree to the education of the life science faculty to the potential of automatic computers and related models for their fields. We feel that many biologists will accept the challenge posed in this context, when assured adequate guidance.

There are a number of possible logistic problems related to running the programming exercises that will usually make teaching assistants at a very junior level valuable to this course.

Content

Topics (Approximate number of lecture hours in parentheses)	Suggested Problems (These may be presented in the context of a biological problem)
1. Algorithms, flow chart representations. (1)	
2. First principles of an algebraic language. (6)	2a. Mean and standard deviation of a sample.
BASIC, FORTRAN, CAL, PL/I, or ALGOL. Organized so that students may begin programming as soon as possible.	2b. Selection sort.
	2c. Table look-up.
	2d. Linear interpolation in a table.

3. Very simple introduction to numerical calculus. (This <u>can</u> be carried out before the students have had any appreciable instruction in calculus.) (4)	3a. Area under a curve by Simpson's rule. 3b. Euler's method (point-slope).
4. Cautionary discussion of error in calculation, with examples.	3c. Root finding by method of false position.
5. Pseudo-random numbers. Simulation (2)	5. Simulation of the rolling of a die.
6. Introduction to the literature of computer programs. (2)	6. Use of a standard data analysis package such as the BIMD statistical programs. Additional program or programs on topics of special interest to the student.

<u>Introduction to Computing</u>: Alternative 2

This course is a one semester three credit hour introduction to applied computing. While the concern for representation of algorithms and data overlaps that of a first course in computer science (see recommendations of the Association for Computing Machinery, Comm. A.C.M. 11, 1968), our suggestion differs in that the accent is always on application, on problem solving with a digital computer. There are three or four suggested programming exercises in an algebraic language and one or two in special purpose languages suited for biological problems. The course is set primarily for sophomores.

<u>Materials</u>

1. An introductory text on computing.
2. References for elementary numerical methods and statistical methods.

Faculty

The course must be handled by a specialist in computing, as opposed to alternative 1, although the elective programming exercise could be directed by a teaching assistant from the life sciences.

Facilities

Computing facilities will be required to handle the submittal of approximately 30 batcn process jobs of short duration per student. About 15 console hours on a time-shared remote access computer would be required equivalently.

Content

Topics (Approximate number of lecture hours in parentheses)	Suggested Problems Problems listed under alternative 1 and others, such as
1. The concept of an algorithm: discussion of its connotations. (2)	
2. Representation of algorithms: natural language, flow chart, algebraic language. (2)	
3. Principles of an algebraic language: FORTRAN, PL/I, ALGOL, or a conversational language: BASIC, CAL, etc., as available. Illustrations from simple numerical and statistical methods. (10)	
4. The evaluation of algorithms, logical organization of a computing machine. (5)	4. Test for well formation of string of parentheses.
5. A sampling of computer applications and methods. Simple symbol manipulation, list structures, simulation examples, pseudo-random number generation, a simulation	5a. Generation of Markov chain from transition matrix (presented in behavioral terms) in algebraic language, or a flow simulation in SIMSCRIPT.

language such as SIMSCRIPT, and specific applications from the life sciences. (12)

6. Discussion or demonstration of special computing equipment involving graphical displays or real-time control of experiments.

5b. Elective problem on a topic from the life sciences such as an epidemic simulation, or the analysis of data from an actual experiment.

5c. Numerical integration, or linear regression with printer plot of graphical output.